



SEQUENCE LISTING

<110> BLACK, Roy A.
PAXTON, Raymond J.
BODE, Wolfram
NASKOS, Klaus
FERNANDEZ-CATALAN, Carlos
CHEN, James Ming
LEVIN, Jeremy Ian

<120> Crystalline TNF-alpha-converting enzyme
and uses thereof

<130> 16163-039004

<140> US 10/784,300
<141> 2004-02-24

<150> US 09/244,984
<151> 1999-02-04

<150> US 60/073,709
<151> 1998-02-04

<150> US 60/135,499
<151> 1998-03-30

<150> US 60/117,476
<151> 1999-01-27

<160> 10

<170> FastSEQ for Windows Version 4.0

<210> 1
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<212> PRT
<213> Artificial Sequence

<220>
<223> Illustrative peptide

<400> 1
Pro Leu Ala Gln Ala Val Arg Ser Ser Ser
1 5 10

<210> 2
<211> 8
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<213> Artificial Sequence

<220>
<223> Illustrative peptide

<400> 2

Gly Ser His His His His His His

1

5

<210> 3

<211> 11

<212> PRT

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<220>

<223> Consensus motif

<220>

<221> VARIANT

<222> 3, 4, 6, 7, 9, 10

<223> Xaa = any amino acid

<400> 3

His Glu Xaa Xaa His Xaa Xaa Gly Xaa Xaa His

1

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<210> 4

<211> 203

<212> PRT

<213> Crotalus adamanteus

<400> 4

Glu Gln Asn Leu Pro Gln Arg Tyr Ile Glu Leu Val Val Val Ala Asp

1

5

10

15

Arg Arg Val Phe Met Lys Tyr Asn Ser Asp Leu Asn Ile Ile Arg Thr

20

25

30

Arg Val His Glu Ile Val Asn Ile Ile Asn Glu Phe Tyr Arg Ser Leu

35

40

45

Asn Ile Arg Val Ser Leu Thr Asp Leu Glu Ile Trp Ser Gly Gln Asp

50

55

60

Phe Ile Thr Ile Gln Ser Ser Ser Ser Asn Thr Leu Asn Ser Phe Gly

65

70

75

80

Glu Trp Arg Glu Arg Val Leu Leu Thr Arg Lys Arg His Asp Asn Ala

85

90

95

Gln Leu Leu Thr Ala Ile Asn Phe Glu Gly Lys Ile Ile Gly Lys Ala

100

105

110

Tyr Thr Ser Ser Met Cys Asn Pro Arg Ser Ser Val Gly Ile Val Lys

115

120

125

Asp His Ser Pro Ile Asn Leu Leu Val Ala Val Thr Met Ala His Glu

130

135

140

Leu Gly His Asn Leu Gly Met Glu His Asp Gly Lys Asp Cys Leu Arg

145

150

155

160

Gly Ala Ser Leu Cys Ile Met Arg Pro Gly Leu Thr Pro Gly Arg Ser

165

170

175

Tyr Glu Phe Ser Asp Asp Ser Met Gly Tyr Tyr Gln Lys Phe Leu Asn

180

185

190

Gln Tyr Lys Pro Gln Cys Ile Leu Asn Lys Pro

195

200

<210> 5
 <211> 287
 <212> PRT
 <213> Homo sapiens

<400> 5

Pro	Glu	Glu	Leu	Val	His	Arg	Val	Lys	Arg	Arg	Ala	Asp	Pro	Asp	Pro
1				5					10					15	
Met	Lys	Asn	Thr	Cys	Lys	Leu	Leu	Val	Val	Ala	Asp	His	Arg	Phe	Tyr
			20					25					30		
Arg	Tyr	Met	Gly	Arg	Gly	Glu	Glu	Ser	Thr	Thr	Thr	Asn	Tyr	Leu	Ile
		35					40					45			
Glu	Leu	Ile	Asp	Arg	Val	Asp	Asp	Ile	Tyr	Arg	Asn	Thr	Ser	Trp	Asp
	50					55					60				
Asn	Ala	Gly	Phe	Lys	Gly	Tyr	Gly	Ile	Gln	Ile	Glu	Gln	Ile	Arg	Ile
65					70				75					80	
Leu	Lys	Ser	Pro	Gln	Glu	Val	Lys	Pro	Gly	Glu	Lys	His	Tyr	Asn	Met
				85				90						95	
Ala	Lys	Ser	Tyr	Pro	Asn	Glu	Glu	Lys	Asp	Ala	Trp	Asp	Val	Lys	Met
			100					105					110		
Leu	Leu	Glu	Gln	Phe	Ser	Phe	Asp	Ile	Ala	Glu	Glu	Ala	Ser	Lys	Val
		115					120					125			
Cys	Leu	Ala	His	Leu	Phe	Thr	Tyr	Gln	Asp	Phe	Asp	Met	Gly	Thr	Leu
	130					135					140				
Gly	Leu	Ala	Tyr	Val	Gly	Ser	Pro	Arg	Ala	Asn	Ser	His	Gly	Gly	Val
145					150					155					160
Cys	Pro	Lys	Ser	Gly	Ser	Ser	Gly	Gly	Ile	Cys	Glu	Lys	Ala	Tyr	Tyr
				165				170						175	
Ser	Pro	Val	Gly	Lys	Lys	Asn	Ser	Lys	Leu	Tyr	Ser	Asp	Gly	Lys	Lys
			180					185					190		
Lys	Glu	Ala	Asp	Leu	Val	Thr	Thr	His	Glu	Leu	Gly	His	Asn	Phe	Gly
		195					200					205			
Ala	Glu	His	Asp	Pro	Asp	Gly	Leu	Ala	Glu	Cys	Ala	Pro	Asn	Glu	Asp
	210					215					220				
Gln	Gly	Gly	Lys	Tyr	Val	Met	Tyr	Pro	Ile	Ala	Val	Ser	Gly	Asp	His
225					230					235					240
Glu	Asn	Asn	Lys	Met	Phe	Ser	Asn	Cys	Ser	Lys	Gln	Ser	Ile	Tyr	Lys
				245				250						255	
Thr	Ile	Glu	Ser	Lys	Ala	Gln	Glu	Cys	Phe	Gln	Glu	Arg	Ser	Asn	Lys
			260				265						270		
Val	Cys	Gly	Asn	Ser	Arg	Val	Asp	Glu	Gly	Glu	Glu	Cys	Asp	Pro	
		275					280					285			

<210> 6
 <211> 276
 <212> PRT
 <213> Homo sapiens

<400> 6

Gln	Glu	Lys	His	Ala	Ile	Asn	Gly	Pro	Glu	Leu	Leu	Arg	Lys	Arg	Arg
1				5					10					15	
Thr	Thr	Ser	Ala	Glu	Lys	Asn	Thr	Cys	Gln	Leu	Tyr	Ile	Gln	Thr	Asp
			20					25					30		
His	Leu	Phe	Phe	Lys	Tyr	Tyr	Gly	Thr	Arg	Glu	Ala	Val	Ile	Ala	Gln
		35					40					45			
Ile	Ser	Ser	His	Val	Lys	Ala	Ile	Asp	Thr	Ile	Tyr	Gln	Thr	Thr	Asp

50		55		60
Phe Ser Gly Ile Arg Asn Ile Ser Phe Met Val Lys Arg Ile Arg Ile				
65		70		75
Asn Thr Thr Ala Asp Glu Lys Asp Pro Thr Asn Pro Phe Arg Phe Pro				
	85		90	95
Asn Ile Ser Val Glu Lys Phe Leu Glu Leu Asn Ser Glu Gln Asn His				
	100		105	110
Asp Asp Tyr Cys Leu Ala Tyr Val Phe Thr Asp Arg Asp Phe Asp Asp				
	115		120	125
Gly Val Leu Gly Leu Ala Trp Val Gly Ala Pro Ile Tyr Leu Asn Ser				
	130		135	140
Gly Leu Thr Ser Thr Ser Leu Asn Thr Gly Ile Ile Thr Val Lys Asn				
	145		150	155
Tyr Gly Lys Thr Ile Leu Thr Lys Gln Asn Tyr Gly Ser His Val Pro				
	165		170	175
Pro Lys Val Ser His Ile Thr Phe Ala His Glu Val Gly His Asn Phe				
	180		185	190
Gly Ser Pro His Asp Ser Gly Thr Glu Cys Thr Pro Gly Glu Ser Lys				
	195		200	205
Asn Leu Gly Gln Lys Glu Asn Gly Asn Tyr Ile Met Tyr Ala Arg Ala				
	210		215	220
Thr Ser Gly Asp Lys Leu Asn Asn Asn Lys Phe Ser Leu Cys Ser Ile				
	225		230	235
Arg Asn Ile Ser Gln Val Leu Glu Lys Lys Arg Asn Asn Cys Phe Val				
	245		250	255
Glu Ser Gly Gln Pro Ile Cys Gly Asn Gly Met Val Glu Gln Gly Glu				
	260		265	270
Glu Cys Asp Cys				
	275			

<210> 7
 <211> 824
 <212> PRT
 <213> Homo sapiens

<400> 7
Met Arg Gln Ser Leu Leu Phe Leu Thr Ser Val Val Pro Phe Val Leu
1 5 10 15
Ala Pro Arg Pro Pro Asp Asp Pro Gly Phe Gly Pro His Gln Arg Leu
20 25 30
Glu Lys Leu Asp Ser Leu Leu Ser Asp Tyr Asp Ile Leu Ser Leu Ser
35 40 45
Asn Ile Gln Gln His Ser Val Arg Lys Arg Asp Leu Gln Thr Ser Thr
50 55 60
His Val Glu Thr Leu Leu Thr Phe Ser Ala Leu Lys Arg His Phe Lys
65 70 75 80
Leu Tyr Leu Thr Ser Ser Thr Glu Arg Phe Ser Gln Asn Phe Lys Val
85 90 95
Val Val Val Asp Gly Lys Asn Glu Ser Glu Tyr Thr Ala Lys Trp Gln
100 105 110
Asp Phe Phe Thr Gly His Val Val Gly Glu Pro Asp Ser Arg Val Leu
115 120 125
Ala His Ile Arg Asp Asp Asp Val Ile Ile Arg Ile Asn Thr Asp Gly
130 135 140
Ala Glu Tyr Asn Ile Glu Pro Leu Trp Arg Phe Val Asn Asp Thr Lys
145 150 155 160

Asp	Lys	Arg	Met	Leu	Val	Tyr	Lys	Ser	Glu	Asp	Ile	Lys	Asn	Val	Ser		
			165						170					175			
Arg	Leu	Gln	Ser	Pro	Lys	Val	Cys	Gly	Tyr	Leu	Lys	Val	Asp	Asn	Glu		
			180					185					190				
Glu	Leu	Leu	Pro	Lys	Gly	Leu	Val	Asp	Arg	Glu	Pro	Pro	Glu	Glu	Leu		
		195					200					205					
Val	His	Arg	Val	Lys	Arg	Arg	Ala	Asp	Pro	Asp	Pro	Met	Lys	Asn	Thr		
	210					215					220						
Cys	Lys	Leu	Leu	Val	Val	Ala	Asp	His	Arg	Phe	Tyr	Arg	Tyr	Met	Gly		
225					230					235					240		
Arg	Gly	Glu	Glu	Ser	Thr	Thr	Thr	Asn	Tyr	Leu	Ile	Glu	Leu	Ile	Asp		
				245					250					255			
Arg	Val	Asp	Asp	Ile	Tyr	Arg	Asn	Thr	Ser	Trp	Asp	Asn	Ala	Gly	Phe		
			260					265					270				
Lys	Gly	Tyr	Gly	Ile	Gln	Ile	Glu	Gln	Ile	Arg	Ile	Leu	Lys	Ser	Pro		
		275					280					285					
Gln	Glu	Val	Lys	Pro	Gly	Glu	Lys	His	Tyr	Asn	Met	Ala	Lys	Ser	Tyr		
	290					295					300						
Pro	Asn	Glu	Glu	Lys	Asp	Ala	Trp	Asp	Val	Lys	Met	Leu	Leu	Glu	Gln		
305					310					315					320		
Phe	Ser	Phe	Asp	Ile	Ala	Glu	Glu	Ala	Ser	Lys	Val	Cys	Leu	Ala	His		
				325					330					335			
Leu	Phe	Thr	Tyr	Gln	Asp	Phe	Asp	Met	Gly	Thr	Leu	Gly	Leu	Ala	Tyr		
			340					345					350				
Val	Gly	Ser	Pro	Arg	Ala	Asn	Ser	His	Gly	Gly	Val	Cys	Pro	Lys	Ala		
		355					360					365					
Tyr	Tyr	Ser	Pro	Val	Gly	Lys	Lys	Asn	Ile	Tyr	Leu	Asn	Ser	Gly	Leu		
	370					375					380						
Thr	Ser	Thr	Lys	Asn	Tyr	Gly	Lys	Thr	Ile	Leu	Thr	Lys	Glu	Ala	Asp		
385					390					395					400		
Leu	Val	Thr	Thr	His	Glu	Leu	Gly	His	Asn	Phe	Gly	Ala	Glu	His	Asp		
				405					410					415			
Pro	Asp	Gly	Leu	Ala	Glu	Cys	Ala	Pro	Asn	Glu	Asp	Gln	Gly	Gly	Lys		
			420					425					430				
Tyr	Val	Met	Tyr	Pro	Ile	Ala	Val	Ser	Gly	Asp	His	Glu	Asn	Asn	Lys		
		435					440					445					
Met	Phe	Ser	Asn	Cys	Ser	Lys	Gln	Ser	Ile	Tyr	Lys	Thr	Ile	Glu	Ser		
	450					455					460						
Lys	Ala	Gln	Glu	Cys	Phe	Gln	Glu	Arg	Ser	Asn	Lys	Val	Cys	Gly	Asn		
465					470					475					480		
Ser	Arg	Val	Asp	Glu	Gly	Glu	Glu	Cys	Asp	Pro	Gly	Ile	Met	Tyr	Leu		
				485					490					495			
Asn	Asn	Asp	Thr	Cys	Cys	Asn	Ser	Asp	Cys	Thr	Leu	Lys	Glu	Gly	Val		
			500					505					510				
Gln	Cys	Ser	Asp	Arg	Asn	Ser	Pro	Cys	Cys	Lys	Asn	Cys	Gln	Phe	Glu		
		515					520					525					
Thr	Ala	Gln	Lys	Lys	Cys	Gln	Glu	Ala	Ile	Asn	Ala	Thr	Cys	Lys	Gly		
	530					535					540						
Val	Ser	Tyr	Cys	Thr	Gly	Asn	Ser	Ser	Glu	Cys	Pro	Pro	Pro	Gly	Asn		
545					550					555					560		
Ala	Glu	Asn	Asp	Thr	Val	Cys	Leu	Asp	Leu	Gly	Lys	Cys	Lys	Asp	Gly		
				565					570					575			
Lys	Cys	Ile	Pro	Phe	Cys	Glu	Arg	Glu	Gln	Gln	Leu	Glu	Ser	Cys	Ala		
			580					585					590				
Cys	Asn	Glu	Thr	Asp	Asn	Ser	Cys	Lys	Val	Cys	Cys	Arg	Asp	Leu	Ser		
		595				600						605					
Gly	Arg	Cys	Val	Pro	Tyr	Val	Asp	Ala	Glu	Gln	Lys	Asn	Leu	Phe	Leu		

610		615		620
Arg Lys Gly Lys Pro Cys Thr Val Gly Phe Cys Asp Met Asn Gly Lys				
625		630		640
Cys Glu Lys Arg Val Gln Asp Val Ile Glu Arg Phe Trp Asp Phe Ile				
	645		650	655
Asp Gln Leu Ser Ile Asn Thr Phe Gly Lys Phe Leu Ala Asp Asn Ile				
	660		665	670
Val Gly Ser Val Leu Val Phe Ser Leu Ile Phe Trp Ile Pro Phe Ser				
	675		680	685
Ile Leu Val His Cys Val Asp Lys Lys Leu Asp Lys Gln Tyr Glu Ser				
	690		695	700
Leu Ser Leu Phe His Pro Ser Asn Val Glu Met Leu Ser Ser Met Asp				
705		710		720
Ser Ala Ser Val Arg Ile Ile Lys Pro Phe Pro Ala Pro Gln Thr Pro				
	725		730	735
Gly Arg Leu Gln Pro Ala Pro Val Ile Pro Ser Ala Pro Ala Ala Pro				
	740		745	750
Lys Leu Asp His Gln Arg Met Asp Thr Ile Gln Glu Asp Pro Ser Thr				
	755		760	765
Asp Ser His Met Asp Glu Asp Gly Phe Glu Lys Asp Pro Phe Pro Asn				
	770		775	780
Ser Ser Thr Ala Ala Lys Ser Phe Glu Asp Leu Thr Asp His Pro Val				
785		790		800
Ala Arg Ser Glu Lys Ala Ala Ser Phe Lys Leu Gln Arg Gln Asn Arg				
	805		810	815
Val Asn Ser Lys Glu Thr Glu Cys				
	820			

<210> 8

<211> 477

<212> PRT

<213> Homo sapiens

<400> 8

Met Arg Gln Ser Leu Leu Phe Leu Thr Ser Val Val Pro Phe Val Leu				
1		5		10
Ala Pro Arg Pro Pro Asp Asp Pro Gly Phe Gly Pro His Gln Arg Leu				
	20		25	30
Glu Lys Leu Asp Ser Leu Leu Ser Asp Tyr Asp Ile Leu Ser Leu Ser				
	35		40	45
Asn Ile Gln Gln His Ser Val Arg Lys Arg Asp Leu Gln Thr Ser Thr				
	50		55	60
His Val Glu Thr Leu Leu Thr Phe Ser Ala Leu Lys Arg His Phe Lys				
65		70		75
Leu Tyr Leu Thr Ser Ser Thr Glu Arg Phe Ser Gln Asn Phe Lys Val				
	85		90	95
Val Val Val Asp Gly Lys Asn Glu Ser Glu Tyr Thr Val Lys Trp Gln				
	100		105	110
Asp Phe Phe Thr Gly His Val Val Gly Glu Pro Asp Ser Arg Val Leu				
	115		120	125
Ala His Ile Arg Asp Asp Asp Val Ile Ile Arg Ile Asn Thr Asp Gly				
	130		135	140
Ala Glu Tyr Asn Ile Glu Pro Leu Trp Arg Phe Val Asn Asp Thr Lys				
145		150		155
Asp Lys Arg Met Leu Val Tyr Lys Ser Glu Asp Ile Lys Asn Val Ser				
	165		170	175

Arg	Leu	Gln	Ser	Pro	Lys	Val	Cys	Gly	Tyr	Leu	Lys	Val	Asp	Asn	Glu	
			180					185					190			
Glu	Leu	Leu	Pro	Lys	Gly	Leu	Val	Asp	Arg	Glu	Pro	Pro	Glu	Glu	Leu	
		195					200					205				
Val	His	Arg	Val	Lys	Arg	Arg	Ala	Asp	Pro	Asp	Pro	Met	Lys	Asn	Thr	
	210					215					220					
Cys	Lys	Leu	Leu	Val	Val	Ala	Asp	His	Arg	Phe	Tyr	Arg	Tyr	Met	Gly	
225					230					235					240	
Arg	Gly	Glu	Glu	Ser	Thr	Thr	Thr	Asn	Tyr	Leu	Ile	Glu	Leu	Ile	Asp	
				245					250					255		
Arg	Val	Asp	Asp	Ile	Tyr	Arg	Asn	Thr	Ser	Trp	Asp	Asn	Ala	Gly	Phe	
		260						265					270			
Lys	Gly	Tyr	Gly	Ile	Gln	Ile	Glu	Gln	Ile	Arg	Ile	Leu	Lys	Ser	Pro	
		275					280					285				
Gln	Glu	Val	Lys	Pro	Gly	Glu	Lys	His	Tyr	Asn	Met	Ala	Lys	Ser	Tyr	
	290					295					300					
Pro	Asn	Glu	Glu	Lys	Asp	Ala	Trp	Asp	Val	Lys	Met	Leu	Leu	Glu	Gln	
305					310					315					320	
Phe	Ser	Phe	Asp	Ile	Ala	Glu	Glu	Ala	Ser	Lys	Val	Cys	Leu	Ala	His	
			325					330					335			
Leu	Phe	Thr	Tyr	Gln	Asp	Phe	Asp	Met	Gly	Thr	Leu	Gly	Leu	Ala	Tyr	
		340					345					350				
Val	Gly	Ser	Pro	Arg	Ala	Asn	Ser	His	Gly	Gly	Val	Cys	Pro	Lys	Ala	
	355					360					365					
Tyr	Tyr	Ser	Pro	Val	Gly	Lys	Lys	Asn	Ile	Tyr	Leu	Asn	Ser	Gly	Leu	
	370				375						380					
Thr	Ser	Thr	Lys	Asn	Tyr	Gly	Lys	Thr	Ile	Leu	Thr	Lys	Glu	Ala	Asp	
385					390					395					400	
Leu	Val	Thr	Thr	His	Glu	Leu	Gly	His	Asn	Phe	Gly	Ala	Glu	His	Asp	
			405					410					415			
Pro	Asp	Gly	Leu	Ala	Glu	Cys	Ala	Pro	Asn	Glu	Asp	Gln	Gly	Gly	Lys	
		420					425					430				
Tyr	Val	Met	Tyr	Pro	Ile	Ala	Val	Ser	Gly	Asp	His	Glu	Asn	Asn	Lys	
	435					440					445					
Met	Phe	Ser	Asn	Cys	Ser	Lys	Gln	Ser	Ile	Tyr	Lys	Thr	Ile	Glu	Ser	
	450					455				460						
Lys	Ala	Gln	Glu	Cys	Phe	Gln	Glu	Arg	Ser	Asn	Lys	Val				
465					470					475						

<210> 9

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetically generated peptide

<400> 9

Ser Pro Leu Ala Gln Ala Val Arg Ser Ser Ser Arg

1

5

10

<210> 10

<211> 4

<212> PRT

<213> Artificial Sequence

<220>

<223> Illustrative Met-turn located in SEQ ID NOs 5 and
6

<400> 10

Tyr Val Met Tyr

1